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NEWS 4 JUL 28 IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
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=> s glycoconjugate?
L1       31789 GLYCOCONJUGATE?

=> s l1 and targeting
L2         478 L1 AND TARGETING

=> s l2 and therapeutic agent
L3          17 L2 AND THERAPEUTIC AGENT

=> s l3 and modified sugar
L4           0 L3 AND MODIFIED SUGAR

=> s l1 and therapeutic?
L5        1005 L1 AND THERAPEUTIC?

=> s l5 and modified saccharride
L6           0 L5 AND MODIFIED SACCHARRIDE

=> s l5 and galactose
L7          76 L5 AND GALACTOSE

=> s l7 and ketone
L8           0 L7 AND KETONE

=> s l7 and GalNAc
```

```
L9            5 L7 AND GALNAC

=> s l9 and O-linked
L10           0 L9 AND O-LINKED

=> dup remove l9
PROCESSING COMPLETED FOR L9
L11           5 DUP REMOVE L9 (0 DUPLICATES REMOVED)

=> s l11 and pd<20031119
   1 FILES SEARCHED...
   4 FILES SEARCHED...
L12           1 L11 AND PD<20031119

=> d l12 cbib abs

L12  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2005:122585  Document No. 142:217398  Cell-free in vitro glycoconjugation of
     interleukin 2 as therapeutic agent against cancer and AIDS in
     mammal and human.  Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe,
     Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA).  U.S. Pat.
     Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S.
     Ser. No. 360,779.  (English).  CODEN: USXXCO.  APPLICATION: US 2003-410980
     20030409.  PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019;
     US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P
     20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US
     2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009;
     US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB   The invention includes methods and compns. for remodeling a peptide mol.,
     including the addition or deletion of one or more glycosyl groups to a
     peptide, and/or the addition of a modifying group to a peptide.  The method
     uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester
     group-containing saccharide to interleukin 2 peptide, and then conjugate the
     saccharide-linked interleukin 2 with modifying group such as polymer,
     therapeutic moiety, detectable label, toxin, radioisotope,
     targeting moiety and peptide.  The saccharide group comprises
     monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl,
     GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc.  The
     enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic
     glycosyltransferase selected from sialyltransferase,
     galactosyltransferase, glucosyltransferase, GalNAc transferase,
     GlcNAc transferase, fucosyltransferase, mannosyltransferase,
     endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc.
     The substrate is a nucleotide sugar such as UDP-glucose, UDP-
     galactose, UDP-galactosamine, UDP-glucosamine,
     UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose,
     GDP-fucose, CMP-sialic acid and CMP-NeuAc.


=> s l2 and 2-N-Acetamidosugars
L13           1 L2 AND 2-N-ACETAMIDOSUGARS

=> d l13 cbib abs

L13  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2001:52655  Document No. 134:248403  Ketone Isosteres of 2-N
     -Acetamidosugars as Substrates for Metabolic Cell Surface
     Engineering.  Hang, Howard C.; Bertozzi, Carolyn R. (Departments of
     Chemistry, University of California, Berkeley, CA, 94720, USA).  Journal
     of the American Chemical Society, 123(6), 1242-1243 (English) 2001.
     CODEN: JACSAT.  ISSN: 0002-7863.  OTHER SOURCES: CASREACT 134:248403.
     Publisher: American Chemical Society.
```

AB Metabolic oligosaccharide engineering using unnatural substrates has provided an avenue for the introduction of novel chemical reactivity on cell surfaces. This approach exploits the unnatural substrate tolerance of enzymes involved in carbohydrate biosynthesis. For example, derivs. of N-acetylmannosamine (ManNAc) which bear a selectively reactive chemical handle, such as a ketone or azide, on the N-acyl group are transformed into glycoconjugate-bound sialosides by human cells. The selective reactivity of ketones with aminooxy or hydrazide groups, and azides with modified phosphine reagents, permits exogenous chemical cell surface targeting. If the substrate promiscuity exhibited by the enzymes and transporters of the sialic acid pathway is a general feature of other carbohydrate metabolic pathways, multiple avenues for metabolic engineering will be available. So far, few studies have addressed the unnatural substrate tolerance of other carbohydrate biosynthetic pathways. The ubiquitous presence of the 2-N-acetamidosugars, N-acetylglucosamine (GlcNAc) and N-acetylgalactosamine (GalNAc), in glycoproteins, proteoglycans, and glycolipids makes them attractive targets for metabolic engineering. GlcNAc and GalNAc are converted within cells to their UDP-activated analogs via salvage pathways. UDP-GlcNAc can be subsequently converted to ManNAc or UDP-GalNAc, or utilized by GlcNAc transferases that incorporate the sugar into various glycoconjugates. Likewise, GalNAc transferases utilize UDP-GalNAc as a substrate and deliver the sugar to numerous glycoconjugates. We considered the possibility that unnatural GlcNAc and GalNAc derivs. might gain access to the cell surface through their resp. salvage pathways. We designed 2-ketosugars, which are C2-carbon isosteres of the 2-N-acetamidosugars , as novel analogs that possess a ketone group for chemoselective reaction with aminooxy or hydrazide reagents. A concise synthesis of 2-ketosugars was developed from known 2-iodosugars, which are readily available by electrophilic iodination of com. available glycals. The cellular metabolism of the 2-ketosugars was investigated in a number of cell lines which exhibit varying patterns of N- and O-linked glycosylation. In conclusion, we have demonstrated that a 2-keto isostere of GalNAc is a novel substrate for metabolic glycoprotein engineering in wild-type and ldl-D CHO cells. The corresponding GlcNAc analog could not be detected on cells of any type, perhaps due to competition with endogenous GlcNAc and its downstream intermediates in the salvage pathway which are present at notoriously high intracellular concns. The 2-keto GalNAc analog should be incorporated into secreted glycoproteins as well as cell surface mols., since both are similarly post-translationally modified. This technique might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification.

```
=> s l2 and ketone
L14             9 L2 AND KETONE

=> s l14 and C-2 position
L15             0 L14 AND C-2 POSITION

=> s l14 and 2N-acetyl
L16             0 L14 AND 2N-ACETYL

=> dup remove l14
PROCESSING COMPLETED FOR L14
L17             5 DUP REMOVE L14 (4 DUPLICATES REMOVED)

=> d l17 1-5 cbib abs

L17  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2008 ACS on STN
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2007:321112 Document No. 146:517239 Direct Identification of Nonreducing GlcNAc Residues on N-Glycans of Glycoproteins Using a Novel Chemoenzymatic Method. Boeggeman, Elizabeth; Ramakrishnan, Boopathy; Kilgore, Charlton; Khidekel, Nelly; Hsieh-Wilson, Linda C.; Simpson, John T.; Qasba, Pradman K. (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, MD, 21702, USA). Bioconjugate Chemistry, 18(3), 806-814 (English) 2007. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB The mutant β1,4-galactosyltransferase (β4Gal-T1), β4Gal-T1-Y289L, in contrast to wild-type β4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, β4Gal-T1-Y289L, to produce glycoconjugates carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technol. such as the possibilities to link cargo mols. to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glyco-targeting of drugs to the site of action or used as biol. probes.

L17 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

2001:52655 Document No. 134:248403 Ketone Isosteres of 2-N-Acetamidosugars as Substrates for Metabolic Cell Surface Engineering. Hang, Howard C.; Bertozzi, Carolyn R. (Departments of Chemistry, University of California, Berkeley, CA, 94720, USA). Journal of the American Chemical Society, 123(6), 1242-1243 (English) 2001. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CASREACT 134:248403. Publisher: American Chemical Society.

AB Metabolic oligosaccharide engineering using unnatural substrates has provided an avenue for the introduction of novel chemical reactivity on cell surfaces. This approach exploits the unnatural substrate tolerance of enzymes involved in carbohydrate biosynthesis. For example, derivs. of N-acetylmannosamine (ManNAc) which bear a selectively reactive chemical handle, such as a ketone or azide, on the N-acyl group are transformed into glycoconjugate-bound sialosides by human cells. The selective reactivity of ketones with aminooxy or hydrazide groups, and azides with modified phosphine reagents, permits exogenous chemical cell surface targeting. If the substrate promiscuity exhibited by the enzymes and transporters of the sialic acid pathway is a general feature of other carbohydrate metabolic pathways, multiple avenues for metabolic engineering will be available. So far, few studies have addressed the unnatural substrate tolerance of other carbohydrate biosynthetic pathways. The ubiquitous presence of the 2-N-acetamidosugars, N-acetylglucosamine (GlcNAc) and N-acetylgalactosamine (GalNAc), in glycoproteins, proteoglycans, and glycolipids makes them attractive targets for metabolic engineering. GlcNAc and GalNAc are converted within cells to their UDP-activated analogs via salvage pathways. UDP-GlcNAc can be subsequently converted to ManNAc or UDP-GalNAc, or utilized by GlcNAc transferases that incorporate the sugar into various glycoconjugates. Likewise, GalNAc transferases utilize UDP-GalNAc as a substrate and deliver the sugar to

numerous glycoconjugates. We considered the possibility that unnatural GlcNAc and GalNAc derivs. might gain access to the cell surface through their resp. salvage pathways. We designed 2-ketosugars, which are C2-carbon isosteres of the 2-N-acetamidosugars, as novel analogs that possess a ketone group for chemoselective reaction with aminooxy or hydrazide reagents. A concise synthesis of 2-ketosugars was developed from known 2-iodosugars, which are readily available by electrophilic iodination of com. available glycals. The cellular metabolism of the 2-ketosugars was investigated in a number of cell lines which exhibit varying patterns of N- and O-linked glycosylation. In conclusion, we have demonstrated that a 2-keto isostere of GalNAc is a novel substrate for metabolic glycoprotein engineering in wild-type and ldl-D CHO cells. The corresponding GlcNAc analog could not be detected on cells of any type, perhaps due to competition with endogenous GlcNAc and its downstream intermediates in the salvage pathway which are present at notoriously high intracellular concns. The 2-keto GalNAc analog should be incorporated into secreted glycoproteins as well as cell surface mols., since both are similarly post-translationally modified. This technique might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification.

L17 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 1
2002001735. PubMed ID: 11750762. Kinetic parameters for small-molecule drug delivery by covalent cell surface targeting. Nauman D A; Bertozzi C R. (Department of Chemistry, University of California-Berkeley, Berkeley, CA 94720, USA.) Biochimica et biophysica acta, (2001 Dec 5) Vol. 1568, No. 2, pp. 147-54. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.
AB Human cells incubated with N-levulinoylmannosamine (ManLev) process this unnatural metabolic precursor into N-levulinoyl sialic acid (SiaLev), which is incorporated into cell surface glycoconjugates. A key feature of SiaLev is the presence of a ketone group that can be exploited in chemoselective ligation reactions to deliver small-molecule probes to the cell surface. A mathematical model was developed and tested experimentally to evaluate the prospects of using cell surface ketones as targets for covalent small-molecule drug delivery. We quantified the absolute number of ketone groups displayed on cell surfaces as a function of the concentration of ManLev in the medium. The apparent rate constants for the hydrolysis and disappearance of the cell surface conjugates were determined, as well as the apparent rate constant for the formation of covalent bonds with cell surface ketones. These values and the mathematical model confirm that chemoselective reactions on the cell surface can deliver to cells similar numbers of molecules as antibodies. Thus, cell surface ketones are a potential vehicle for a metabolically controlled small-molecule drug delivery system.

L17 ANSWER 4 OF 5 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
2001150802 EMBASE Biochemical engineering of the N-acyl side chain of sialic acid: Biological implications.
Keppler, O.T.; Horstkorte, R.; Pawlita, M.; Schmidt, C.; Reutter, W. (correspondence). Inst. Molekularbiologie Biochemie, Fachbereich Humanmedizin, Freie Universitat Berlin, Arnimallee 22, D-14195 Berlin-Dahlem, Germany.
Glycobiology Vol. 11, No. 2, pp. 11R-18R 2001.
Refs: 43.
ISSN: 0959-6658. CODEN: GLYCE3.
Pub. Country: United Kingdom. Language: English. Summary Language: English.
Entered STN: 20010510. Last Updated on STN: 20010510

AB N-Acetylneuraminic acid is the most prominent sialic acid in eukaryotes. The structural diversity of sialic acid is exploited by viruses, bacteria, and toxins and by the sialoglycoproteins and sialoglycolipids involved in cell-cell recognition in their highly specific recognition and binding to cellular receptors. The physiological precursor of all sialic acids is N-acetyl D-mannosamine (ManNAc). By recent findings it could be shown that synthetic N-acyl-modified D-mannosamines can be taken up by cells and efficiently metabolized to the respective N-acyl-modified neuraminic acids in vitro and in vivo. Successfully employed D-mannosamines with modified N-acyl side chains include N-propanoyl- (ManNProp), N-butanoyl- (ManNBut)-, N-pentanoyl- (ManNPent), N-hexanoyl- (ManNHex), N-crotonoyl- (ManNCrot), N-levulinoyl- (ManNLev), N-glycolyl-(ManNGc), and N-azidoacetyl D-mannosamine (ManNAc-azido). All of these compounds are metabolized by the promiscuous sialic acid biosynthetic pathway and are incorporated into cell surface sialoglycoconjugates replacing in a cell type-specific manner 10-85% of normal sialic acids. Application of these compounds to different biological systems has revealed important and unexpected functions of the N-acyl side chain of sialic acids, including its crucial role for the interaction of different viruses with their sialylated host cell receptors. Also, treatment with ManNProp, which contains only one additional methylene group compared to the physiological precursor ManNAc, induced proliferation of astrocytes, microglia, and peripheral T-lymphocytes. Unique, chemically reactive ketone and azido groups can be introduced biosynthetically into cell surface sialoglycans using N-acyl-modified sialic acid precursors, a process offering a variety of applications including the generation of artificial cellular receptors for viral gene delivery. This group of novel sialic acid precursors enabled studies on sialic acid modifications on the surface of living cells and has improved our understanding of carbohydrate receptors in their native environment. The biochemical engineering of the side chain of sialic acid offers new tools to study its biological relevance and to exploit it as a tag for therapeutic and diagnostic applications.

L17 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
1997:158946 Engineering novel cell surface chemistry for selective tumor cell targeting.. Bertozzi, Carolyn R. (Lawrence Berkely National Laboratories, University California, Berkeley, CA, 94720, USA). Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17, CARB-013. American Chemical Society: Washington, D. C. (English) 1997. CODEN: 64AOAA.

AB A common feature of many different cancers is the high expression level of the two monosaccharides sialic acid and fucose within the context of cell-surface associated glycoconjugates. A correlation has been made between hypersialylation and/or hyperfucosylation and the highly metastatic phenotype. Thus, a targeting strategy based on sialic acid or fucose expression would be a powerful tool for the development of new cancer cell-selective therapies and diagnostic agents. We have discovered that ketone groups can be incorporated metabolically into cell-surface associated sialic acids. The ketone is chemical unique to the cell surface and can be covalently ligated with hydrazide functionalized proteins or small mols. under physiol. conditions. Thus, we have discovered a mechanism to selectively target hydrazide conjugates to highly sialylated cells such as cancer cells. Applications of this technol. to the generation of novel cancer cell-selective toxins and MRI contrast reagents will be discussed, in addition to progress towards the use of cell surface fucose residues as vehicles for ketone expression.

=> s l2 and galactose
L18 74 L2 AND GALACTOSE

```
=> s l18 and amino group
L19          5 L18 AND AMINO GROUP

=> dup remove l19
PROCESSING COMPLETED FOR L19
L20          1 DUP REMOVE L19 (4 DUPLICATES REMOVED)

=> d l20 cbib abs

L20  ANSWER 1 OF 1     MEDLINE on STN                    DUPLICATE 1
1994264691.    PubMed ID: 8205127.   Tissue-targeting ability of
     saccharide-poly(L-lysine) conjugates. Gonsho A; Irie K; Susaki H; Iwasawa
     H; Okuno S; Sugawara T. (Drug Delivery System Institute, Ltd., Science
     University of Tokyo, Chiba, Japan. ) Biological & pharmaceutical bulletin,
     (1994 Feb) Vol. 17, No. 2, pp. 275-82.  Journal code: 9311984. ISSN:
     0918-6158. Pub. country: Japan. Language: English.
AB   To evaluate the effect of introducing a saccharide moiety to poly(amino
     acids) on tissue distribution, several glycoconjugates of
     epsilon-(2-methoxyethoxyacetyl)-poly(L-lysine) of three molecular weights
     were synthesized using an octylene spacer between the sugar and polymer
     chain.  Methoxyethoxyacetylation of the epsilon-amino
     group of the lysine unit in poly(L-lysine) was useful for avoiding
     nonspecific distribution to many tissues as the result of cationic
     charges.  The tissue-targeting ability of each saccharide moiety
     was considered as the actual amount changed in each tissue caused by
     saccharide modification.  Galactose terminated saccharides such
     as galactose, lactose and N-acetylgalactosamine accumulated
     exclusively in the liver, probably by the hepatic receptor.  These
     conjugates could therefore be good carriers for a drug delivery system to
     the liver.  On the other hand, the mannosyl and fucosyl conjugates were
     preferentially delivered to the reticuloendothelial systems such as those
     in the liver, spleen and bone marrow.  In particular, fucosyl conjugates
     accumulated more in the bone marrow than in the spleen.  Xylosyl
     conjugates accumulated mostly in the liver and lung.  Generally, the
     accumulated amount in the target tissue increased with increasing
     molecular weight and an increased number of saccharides on one molecule of
     polymer.


=> s l18 and hydroxyl group
L21          0 L18 AND HYDROXYL GROUP

=> s l18 and carboxyl
L22          1 L18 AND CARBOXYL

=> d l22 cbib abs

L22  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2005:122585   Document No. 142:217398  Cell-free in vitro glycoconjugation of
     interleukin 2 as therapeutic agent against cancer and AIDS in mammal and
     human.  Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes,
     David; Chen, Xi (Neose Technologies, Inc., USA).  U.S. Pat. Appl. Publ. US
     20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779.
     (English).  CODEN: USXXCO.  APPLICATION: US 2003-410980 20030409.
     PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US
     2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607;
     US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P
     20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US
     2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB   The invention includes methods and compns. for remodeling a peptide mol.,
     including the addition or deletion of one or more glycosyl groups to a
```

peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, targeting moiety and peptide. The saccharide group comprises monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-galactose, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

```
=> s l18 and hydroxyl
L23          0 L18 AND HYDROXYL

=> s l18 and thiol
L24          0 L18 AND THIOL

=> s l18 and phosphate
L25          6 L18 AND PHOSPHATE

=> dup remove l25
PROCESSING COMPLETED FOR L25
L26            6 DUP REMOVE L25 (0 DUPLICATES REMOVED)

=> d l26 1-6 cbib abs

L26  ANSWER 1 OF 6  EMBASE  COPYRIGHT (c) 2008 Elsevier B.V. All rights
     reserved on STN
2007034665  EMBASE  Oligosaccharides, neoglycoproteins and humanized plastics:
     Their biocatalytic synthesis and possible medical applications.
     Nahalka, Jozef (correspondence); Gemeiner, Peter. Institute of Chemistry,
     Slovak Academy of Sciences, Dubravska cesta 9, SK-845 38 Bratislava,
     Slovakia. nahalka@savba.sk. Shao, Jun. Ilypsa, Inc., 3406 Central
     Expressway, Santa Clara, CA 95051, United States.
     Biotechnology and Applied Biochemistry  Vol. 46, No. 1, pp. 1-12  Jan
     2007.
     Refs: 97.
     ISSN: 0885-4513. CODEN: BABIEC.
     Pub. Country: United Kingdom. Language: English. Summary Language:
     English.
     Entered STN: 20070220. Last Updated on STN: 20070220
AB   Glycobiology has become one of the fastest growing branches of the
     biological sciences.  Glycomics, which is the study of an organism's
     entire array of oligosaccharides, is now emerging as the third informatics
     wave after genomics and proteomics.  For example, it is possible to see
     this progress in the KEGG (Kyoto Encyclopedia of Genes and Genomes)
     database (http://www.genome.jp/ kegg/pathway/map/map01110.html).  The
     interest in this area stems from the realization that carbohydrates,
     especially oligosaccharides, and their interactions with proteins, play
     diverse informative roles in all organisms, and that more than half of all
     proteins are glycosylated.  When the biological and pharmaceutical
     importance of glycoconjugates is considered, it is surprising
     how little glycobiotechnology has developed.  This review reports the
     latest developments in the biocatalytic synthesis of oligosaccharides and
```

glycoconjugates, with special attention paid to the glycosyltransferase approach. The second part of the review takes the 'conceptual approach' and covers possible medical applications of synthesized glycoconjugates. Various new examples of the conjugation of glyco-informative saccharide sequence to known pharmaceuticals or biomaterials are cited. .COPYRGT. 2007 Portland Press Ltd.

L26 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
2005:216712 Document No. 142:292453 Nanoparticulate complexes of double-stranded nucleic acids and melamine derivatives for delivery of nucleic acids, including siRNA. Quay, Steven C.; Cui, Kunyuan; Dattilo, James W. (Nastech Pharmaceutical Company Inc., USA). PCT Int. Appl. WO 2005021044 A2 20050310, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US27806 20040825. PRIORITY: US 2003-497740P 20030825.

AB Nanoparticles of double-stranded nucleic acid complexed with a complexing agent, especially melamine derivs. 2,4,6-triguanidotriazine (I) and 2,4,6-triamidosarcosylmelamine (II), that form complexes with the nucleic acids are described for delivery of nucleic acids, especially siRNA, to a target organism, e.g. in treatment of disease. Each of these mols. can bind to three phosphate groups, allowing each mol. of I or II to bind up to three mols. of nucleic acids. The complex may be further stabilized by complexing with poly-L-arginine or a copolymer of L-glutamine and L-asparagine. The polyaminoacid may in turn be conjugated with targeting moieties. In a preferred embodiment, the nucleic acid is a double stranded RNA having 15 to 30 base pairs suitable for RNA interference. In another aspect of the invention, a dsRNA is produced in which all of the uridines are changed to 5-methyluridine (ribothymidine.). Preferably, the resultant dsRNAs have 15 to about 30 base pairs and are suitable for RNA interference. Ribothymidine-containing siRNA is effect in gene silencing and is stable to the RNAses of rat blood plasma. Synthesis of the melamine derivs. is described.

L26 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
2005:122585 Document No. 142:217398 Cell-free in vitro glycoconjugation of interleukin 2 as therapeutic agent against cancer and AIDS in mammal and human. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410980 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, targeting moiety and peptide. The saccharide group comprises

monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-galactose, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

L26 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
2004:182383 Document No. 140:231203 Methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Pubi. US 20040043446 A1 20040304, 761 pp., Cont.-in-part of Appl. No. PCT/US02/32263. (English). CODEN: USXXCO. APPLICATION: US 2003-411037 20030409. PRIORITY: US 2002-2002/PV38729U 20020607; US 2002-2002/PV39177U 20020625; US 2002-2002/PV39659U 20020717; US 2002-2002/PV40424U 20020816; US 2002-2002/PV40752W 20020828; WO 2002-US32263 20021009.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The invention claims a method of remodeling an α-galactosidase A peptide in vitro by removing a saccharyl subunit from the peptide and contacting the truncated glycan with at least one glycosyltransferase and a glycosyl donor to transfer the glycosyl donor to the glycan moiety. The glycosyl donor may contain a modifying group such as a polymer, a therapeutic toxin, a detectable label, a reactive linker group, or a targeting mol. The invention specifically claims α-galactosidase glycopeptides containing mannooligosaccharide or sialyloligosaccharide structures and their modification with a galactosyltransferase, a sialyltransferase, or a mannosyltransferase and modified glycosyl donors such as UDP-Gal-polyethylene glycol (PEG)-transferrin , CMP-sialic acid linker-mannose-6-phosphate, CMP-sialic acid-PEG, or GDP-mannose-linker-ApoE. Conjugation of glycopeptides with PEG, for example, is intended to reduce the immunogenicity of peptides and prolong their half-life in circulation. Conjugation of glycopeptides with transferrin is intended to transport glycoconjugates across the blood-brain barrier. In addition, the invention claims therapeutic use of a glycoconjugated α-galactosidase A peptide for Fabry disease. Examples of the invention include synthesis of CMP-sialic acid, UDP-galactose, UDP-glucosamine, and UDP-galactosamine conjugates with polyethylene glycol, sialylation of recombinant glycoproteins antithrombin III, fetuin, and α1-antitrypsin by recombinant rat ST3Gal III, and glyco-remodeling of Cri-IgG1 monoclonal antibody. The general procedure for making UDP-GlcNAc-PEG is that the protected amino sugar diphospho-nucleotide is oxidized to form an aldehyde at the 6-position of the sugar. The aldehyde is converted to the corresponding primary amine by formation and reduction of the Schiff base. The resulting intermediate is contacted with the p-nitrophenol carbonate of m-PEG, which reacts with the amine, binding the m-PEG to the saccharide via an amide bond.

L26 ANSWER 5 OF 6 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
2003458168 EMBASE Specificity and Mechanism of Metal Ion Activation in UDP-galactose:β -Galactoside-α-1,3-galactosyltransferase.
Zhang, Yingnan; Brew, Keith (correspondence). Dept. of Biochem. and Molec. Biology, Univ. of Miami School of Medicine, Miami, FL 33101, United States

. kbrew@fav.edu. Wang, Peng G.. Department of Chemistry, Wayne State University, Detroit, MI 48202, United States. Brew, Keith (correspondence). Dept. of Biomedical Sciences, Florida Atlantic University, 777 Glades Rd., Boca Raton, FL 33431, United States. kbrew@fav.edu.
Journal of Biological Chemistry Vol. 276, No. 15, pp. 11567-11574 13 Apr 2001.
Refs: 48.
ISSN: 0021-9258. CODEN: JBCHA3.
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20031204. Last Updated on STN: 20031204

AB UDP-galactose:β-galactosyl-α1,3-galactosyltransferase (α3GT) catalyzes the synthesis of galactosyl-α-1, 3-β-galactosyl structures in mammalian glycoconjugates. In humans the gene for α3GT is inactivated, and its product, the α-Gal epitope, is the target of a large fraction of natural antibodies. α3GT is a member of a family of metal-dependent-retaining glycosyltransferases that includes the histo blood group A and B enzymes. Mn(2+) activates the catalytic domain of α3GT (α3GTcd), but the affinity reported for this ion is very low relative to physiological levels. Enzyme activity over a wide range of metal ion concentrations indicates a dependence on Mn(2+) binding to two sites. At physiological metal ion concentrations, Zn(2+) gives higher levels of activity and may be the natural cofactor. To determine the role of the cation, metal activation was perturbed by substituting Co (2+) and Zn(2+) for Mn(2+) and by mutagenesis of a conserved D(149)VD(151) sequence motif that is considered to act in cation binding in many glycosyltransferases. The aspartates of this motif were found to be essential for activity, and the kinetic properties of a Val(150) to Ala mutant with reduced activity were determined. The results indicate that the cofactor is involved in binding UDP-galactose and has a crucial influence on catalytic efficiency for galactose transfer and for the low endogenous UDP-galactose hydrolase activity. It may therefore interact with one or more phosphates of UDP-galactose in the Michaelis complex and in the transition state for cleavage of the UDP to galactose bond. The DXD motif conserved in many glycosyltransferases appears to have a key role in metal-mediated donor substrate binding and phosphate-sugar bond cleavage.

L26 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
1987:596522 Document No. 107:196522 Original Reference No. 107:31517a,31520a
The use of glycoside aglycones to control the regioselectivity of glycosidic bond formation during enzymic oligosaccharide synthesis. Nilsson, Kurt (Svenska Sockerfabriks AB, Swed.). Eur. Pat. Appl. EP 226563 A1 19870624, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1986-850414 19861202. PRIORITY: SE 1985-5842 19851211.

AB A method for controlling the regioselectivity of the glycosidic bond formed glycosyl donor and glycosyl acceptor in the enzymic production of an oligosaccharide compound, which either consists of or is a fragment or an analog of the carbohydrate part in a glycoconjugate, by reverse hydrolysis or transglycosidation is described. The method also facilitates purification of the products and facilitates their use in preparation of glycoconjugates (e.g. glycoproteins, glycolipids) which may be used for drug targeting or for diagnosis and treatment of diseases, e.g. cancer. Methyl-3-O-α-D-galactopyranosyl-α-D-galactopyranoside was prepared in 39% yield by the action of coffee bean α-galactosidase (EC 3.2.1.22) on Gal(α-O-p-nitrophenyl and Gal(α)-OMe in an aqueous solution of Na phosphate (pH 6.5) and N,N-dimethylformamide.

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=> s l18 and phosphinate
L27          0 L18 AND PHOSPHINATE

=> s l18 and sulfate
L28          1 L18 AND SULFATE

=> d l28 cbib abs

L28  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2005:122585   Document No. 142:217398  Cell-free in vitro glycoconjugation of
     interleukin 2 as therapeutic agent against cancer and AIDS in mammal and
     human.  Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes,
     David; Chen, Xi (Neose Technologies, Inc., USA).  U.S. Pat. Appl. Publ. US
     20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779.
     (English).  CODEN: USXXCO.  APPLICATION: US 2003-410980 20030409.
     PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US
     2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607;
     US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P
     20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US
     2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB   The invention includes methods and compns. for remodeling a peptide mol.,
     including the addition or deletion of one or more glycosyl groups to a
     peptide, and/or the addition of a modifying group to a peptide.  The method
     uses enzyme to remove or add phosphate, sulfate, carboxylate
     and/or ester group-containing saccharide to interleukin 2 peptide, and then
     conjugate the saccharide-linked interleukin 2 with modifying group such as
     polymer, therapeutic moiety, detectable label, toxin, radioisotope,
     targeting moiety and peptide.  The saccharide group comprises
     monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl,
     GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc.  The enzyme for
     the saccharide addition or removal is a prokaryotic or eukaryotic
     glycosyltransferase selected from sialyltransferase,
     galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc
     transferase, fucosyltransferase, mannosyltransferase,
     endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc.
     The substrate is a nucleotide sugar such as UDP-glucose, UDP-
     galactose, UDP-galactosamine, UDP-glucosamine,
     UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose,
     GDP-fucose, CMP-sialic acid and CMP-NeuAc.


=> s l18 and sulfinate
L29          0 L18 AND SULFINATE

=> s (qasba p?/au or ramakrishnan b?/au)
L30        866 (QASBA P?/AU OR RAMAKRISHNAN B?/AU)

=> s l30 and glycoconjugate?
L31         35 L30 AND GLYCOCONJUGATE?

=> s l31 and target?
L32         14 L31 AND TARGET?

=> dup remove l32
PROCESSING COMPLETED FOR L32
L33          9 DUP REMOVE L32 (5 DUPLICATES REMOVED)

=> d l33 1-9 cbib abs

L33  ANSWER 1 OF 9     MEDLINE on STN                    DUPLICATE 1
2008368926.    PubMed ID: 18426242.   Site-specific linking of biomolecules via
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glycan residues using glycosyltransferases. Qasba Pradman K; Boeggeman Elizabeth; Ramakrishnan Boopathy. (Structural Glycobiology Section, SAIC-Frederick, Inc., Center for Cancer Research Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.. qasba@helix.nih.gov) . Biotechnology progress, (2008 May-Jun) Vol. 24, No. 3, pp. 520-6. Electronic Publication: 2008-04-22. Journal code: 8506292. E-ISSN: 1520-6033. Pub. country: United States. Language: English.

AB The structural information on glycosyltransferases has revealed that the sugar-donor specificity of these enzymes can be broadened to include modified sugars with a chemical handle that can be utilized for conjugation chemistry. Substitution of Tyr289 to Leu in the catalytic pocket of bovine beta-1,4-galactosyltransferase generates a novel glycosyltransferase that can transfer not only Gal but also GalNAc or a C2-modified galactose that has a chemical handle, from the corresponding UDP-derivatives, to the non-reducing end GlcNAc residue of a glycoconjugate. Similarly, the wild-type polypeptide-N-acetyl-galactosaminyltransferase, which naturally transfers GalNAc from UDP-GalNAc, can also transfer C2-modified galactose with a chemical handle from its UDP-derivative to the Ser/Thr residue of a polypeptide acceptor substrate that is tagged as a fusion peptide to a non-glycoprotein. The potential of wild-type and mutant glycosyltransferases to produce glycoconjugates carrying sugar moieties with chemical handle makes it possible to conjugate biomolecules with orthogonal reacting groups at specific sites. This methodology assists in the assembly of bio-nanoparticles that are useful for developing targeted drug-delivery systems and contrast agents for magnetic resonance imaging.

L33 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2008:390303 New synthetic sugar-nucleotide donor substrates for glycosyltransferases. Manzoni, Maria R.; Boeggeman, Elizabeth; Ramakrishnan, Boopathy; Pasek, Marta; Qasba, Pradman Krishen (Structural Glycobiology Section, Nanobiology Program, Center for Cancer Research, National Cancer Institute-NIH, Frederick, MD, 21702-1201, USA). Abstracts of Papers, 235th ACS National Meeting, New Orleans, LA, United States, April 6-10, 2008, ORGN-275. American Chemical Society: Washington, D. C. (English) 2008. CODEN: 69KNN3.

AB Considering the important role of glycoconjugates in biol. recognition, acute and chronic diseases (such as inflammation), and numerous cancer types; methods capable of introducing a sugar residue with a reactive chemical handle at a unique site in the oligosaccharide chain of relevant glycoprotein and/or glycolipid are highly desirable. Structure-based design of novel glycosyltransferases is making it possible to transfer unnatural sugars to specific monosaccharide residue on a glycan chain. These carbohydrates with chemical handles have been shown to be new sugar-donor substrates for natural and engineered mutant glycosyltransferases. While exploiting this selective, chemoenzymic approach, these functionalized, unnatural glycoconjugates have a variety of new diagnostic and therapeutic applications allowing for the incorporation of probes, biomarkers, and/or drug-targeting systems.

L33 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2008:950006 Useful applications of synthetic modified-sugar nucleotide donor substrates. Manzoni, Maria R.; Boeggeman, Elizabeth; Ramakrishnan, Boopathy; Qasba, Pradman Krishen (Structural Glycobiology Section, Nanobiology Program, Center for Cancer Research, National Cancer Institute-NIH, Frederick, MD, 21702-1201, USA). Abstracts of Papers, 236th ACS National Meeting, Philadelphia, PA, United States, August 17-21, 2008, BIOT-167. American Chemical Society: Washington, D. C. (English) 2008. CODEN: 69KXQ2.

AB Considering the important role of glycoconjugates in biol. recognition, acute and chronic diseases (such as inflammation), and numerous cancer types; methods capable of introducing a sugar residue with a reactive chemical handle at a unique site in the oligosaccharide chain of relevant glycoprotein and/or glycolipid are highly desirable. Structure-based design of novel glycosyltransferases is making it possible to transfer unnatural sugars to a specific monosaccharide residue on a glycan chain or directly to a peptide because these carbohydrates with chemical handles have been shown to be new sugar-donor substrates for natural and engineered mutant glycosyltransferases. While exploiting this selective, chemoenzymic approach, these functionalized, unnatural glycoconjugates have a variety of new diagnostic and therapeutic applications allowing for the incorporation of probes, biomarkers, and development of drug-targeting systems. We are currently synthesizing novel unnatural carbohydrates that will contain the functionality for incorporating probes and/or biomarkers; namely, we plan to exploit this technol. for the anal. of "over-" and "under-" glycosylated glycans related to certain disease. These techniques will facilitate the diagnosis of a diseases by tracing of aberrant glycosylation patterns associated with the diseases, as well as the anal. of specific glycoconjugates related to biol. recognition. The usefulness of this conjugation method will be discussed since we have developed mutant glycosyltransferases that are capable of transferring modified sugars to specific monosaccharide residue of therapeutic monoclonal antibodies in a selective, controlled manner. Thus, this technol. is also applicable to drug development.

L33 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
2007:321112 Document No. 146:517239 Direct Identification of Nonreducing GlcNAc Residues on N-Glycans of Glycoproteins Using a Novel Chemoenzymatic Method. Boeggeman, Elizabeth; Ramakrishnan, Boopathy; Kilgore, Charlton; Khidekel, Nelly; Hsieh-Wilson, Linda C.; Simpson, John T.; Qasba, Pradman K. (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, MD, 21702, USA). Bioconjugate Chemistry, 18(3), 806-814 (English) 2007. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB The mutant β1,4-galactosyltransferase (β4Gal-T1), β4Gal-T1-Y289L, in contrast to wild-type β4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, β4Gal-T1-Y289L, to produce glycoconjugates carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technol. such as the possibilities to link cargo mols. to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glyco-targeting of drugs to the site of action or used as biol. probes.

L33 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
2007:879157 Mutant glycosyltransferases assist in linking

glycoconjugates via glycan chains: Development of a targeted drug delivery system and contrast agents for MRI. Qasba, Pradman Krishen; Boeggeman, Elizabeth; Ramakrishnan, Boopathy (Structural Glycobiology Section, Nanobiology Program, Center for Cancer Research, NCI-Frederick, NCI, NIH, Frederick, MD, 21702-1203, USA). Abstracts of Papers, 234th ACS National Meeting, Boston, MA, United States, August 19-23, 2007, BIOT-185. American Chemical Society: Washington, D. C. (English) 2007. CODEN: 69JNR2.

AB The structural information of glycosyltransferases has revealed that the specificity of the sugar donor in these enzymes is determined by a few residues in the sugar-nucleotide binding pocket of the enzyme, conserved among the family members from different species. This in turn has made it possible to reengineer the existing glycosyltransferases with broader sugar donor specificities. Mutation of these residues generates novel glycosyltransferases that can transfer a sugar residue with a chemical reactive functional group to N-acetylglucosamine (GlcNAc), galactose (Gal) and xylose residues of glycoproteins, glycolipids and proteoglycans (glycoconjugates). The potential of mutant glycosyltransferases to produce glycoconjugates carrying sugar moieties with reactive groups which can be used subsequently in the assembly of bio-nanoparticles is making it possible to develop a targeted-drug delivery system and contrast agents for MRI. This project has been funded in whole or in part with federal funds from the NCI, National Institutes of Health, under contract N01-CO-12400.

L33 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2007:520558 Syntheses of unnatural glycoconjugates with vast biological applications. Manzoni, Maria R.; Ramakrishnan, Boopathy; Boeggeman, Elizabeth; Qasba, Pradman K. (Center for Cancer Research-Nanobiology Program, National Cainstitutute-NIH, Frederick, MD, 21702, USA). Abstracts, 39th Middle Atlantic Regional Meeting of the American Chemical Society, Collegeville, PA, United States, May 16-18, MARM-129. American Chemical Society: Washington, D. C. (English) 2007. CODEN: 69JFDW.

AB In view of the important role of glycoconjugates in biol. recognition, acute and chronic diseases (such as inflammation), and numerous cancer types; methods capable of introducing an unnatural sugar at a unique site in the oligosaccharide chain of relevant glycoprotein and/or glycolipid are highly desirable. We have developed mutant glycosyltransferases that are capable of transferring modified sugars to specific monosaccharide residue on a glycan chain. We are currently synthesizing novel unnatural carbohydrates that will contain the functionality for incorporating probes and/or biomarkers. We plan to exploit this technol. for the anal. of "under-" and "over-glycosylated" glycans related to certain disease. These techniques will facilitate the tracing of aberrant glycosylation patterns associated with diseases, as well as the anal. or diagnosis of specific glycoconjugates related to biol. recognition, and drug therapy. In addition, this method may have vast biol. applications, such as the development of targeted drug delivery systems, fluorescent derivitization for glycomic anal., or contrast agents for MRI.

L33 ANSWER 7 OF 9 MEDLINE on STN DUPLICATE 2

2006186546. PubMed ID: 16584127. Mutant glycosyltransferases assist in the development of a targeted drug delivery system and contrast agents for MRI. Qasba Pradman K; Ramakrishnan Boopathy ; Boeggeman Elizabeth. (Structural Glycobiology Section, Nanobiology Program, CCR, NCI-Frederick, Frederick, MD, USA.. qasba@helix.nih.gov) . The AAPS journal, (2006) Vol. 8, No. 1, pp. E190-5. Electronic Publication: 2006-03-24. Ref: 64. Journal code: 101223209. E-ISSN: 1550-7416. Pub. country: United States. Language: English.

AB The availability of structural information on glycosyltransferases is

beginning to make structure-based reengineering of these enzymes possible. Mutant glycosyltransferases have been generated that can transfer a sugar residue with a chemically reactive unique functional group to a sugar moiety of glycoproteins, glycolipids, and proteoglycans (glycoconjugates). The presence of modified sugar moiety on a glycoprotein makes it possible to link bioactive molecules via modified glycan chains, thereby assisting in the assembly of bionanoparticles that are useful for developing the targeted drug delivery system and contrast agents for magnetic resonance imaging. The reengineered recombinant glycosyltransferases also make it possible to (1) remodel the oligosaccharide chains of glycoprotein drugs, and (2) synthesize oligosaccharides for vaccine development.

L33 ANSWER 8 OF 9 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

2006159419 EMBASE Mutant glycosyltransferases assist in the development of a targeted drug delivery system and contrast agents for MRI.

Qasba, Pradman K. (correspondence); Ramakrishnan, Boopathy; Boeggeman, Elizabeth. Structural Glycobiology Section, Nanobiology Program, NCI-Frederick, Building 469, Frederick, MD 21702, United States. qasba@helix.nih.gov. Ramakrishnan, Boopathy; Boeggeman, Elizabeth. Basic Research Program, SAIC-Frederick Inc., Frederick, MD, United States. Qasba, Pradman K. (correspondence) . Structural Glycobiology Section, CCRNP, NCI-Frederick, Building 469, Frederick, MD 21702, United States. qasba@helix.nih.gov.

AAPS Journal Vol. 8, No. 1, pp. E190-E195 24 Mar 2006. arn. 23
Refs: 64.
ISSN: 1550-7416.
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20060412. Last Updated on STN: 20060412

AB The availability of structural information on glycosyltransferases is beginning to make structure-based reengineering of these enzymes possible. Mutant glycosyltransferases have been generated that can transfer a sugar residue with a chemically reactive unique functional group to a sugar moiety of glycoproteins, glycolipids, and proteoglycans (glycoconjugates). The presence of modified sugar moiety on a glycoprotein makes it possible to link bioactive molecules via modified glycan chains, thereby assisting in the assembly of bionanoparticles that are useful for developing the targeted drug delivery system and contrast agents for magnetic resonance imaging. The reengineered recombinant glycosyltransferases also make it possible to (1) remodel the oligosaccharide chains of glycoprotein drugs, and (2) synthesize oligosaccharides for vaccine development.

L33 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2005:490304 Document No. 143:48058 Targeted delivery system for bioactive agents. Qasba, Pradman; Ramakrishnan, Boopathy (ushu, USA). PCT Int. Appl. WO 2005051429 A2 20050609, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US38781 20041118. PRIORITY: US 2003-523112P 20031119.

AB In accordance with the present invention, compds., compns. and methods are provided that allow for the administration of a bioactive agent to an organism, including a human or an animal. The present invention can be

used to treat or prevent a disease and/or disorder with a bioactive agent, or can be used to safely vaccinate a human or animal against a bioactive agent. The invention can also be used as a method for the delivery of bioactive agents for the treatment or prevention of a disease and/or a disorder, particularly targeted delivery of bioactive agents through the administration of glycoconjugates containing a bioactive agent bound to a targeting compound through a modified saccharide residue. A chemoenzymic approach toward the rapid and sensitive detection of O-GlcNAc posttranslational modifications is also described.

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